Notice of Allowability	Application No.	Applicant(s)	
	10/550,778	ZUMBRUNN ET AL.	
	Examiner	Art Unit	
	ANDREW D. KOSAR	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *interview of 6/16/10*.

2. ☒ The allowed claim(s) is/are *40,50-57,61-66,68 and 71*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 2/16/10
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20100617* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

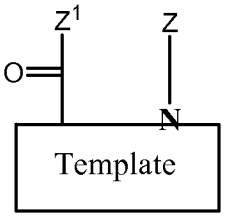
Authorization for this examiner's amendment was given in a telephone interview with Applicant's representative, Andrea Wilkovich on June 16, 2010.

The application has been amended as follows:

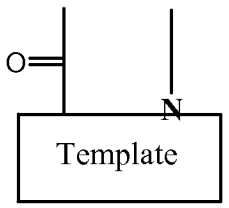
REPLACE the claim set with the following claims.

1-39. (Previously cancelled)

40. (Currently amended) A compound of the general formula



(I)



wherein _____ is selected from the group consisting of ^{D}Pro-^{L}Pro and ^{L}Pro-^{D}Pro; Z and Z^1 are chains of n and, respectively, n' α-amino acid residues whereby either n is 4 and n' is 6 or n is 5 and n' is 7, the positions of said amino acid residues in said chain Z being counted from the N-terminal amino acid and the positions of said amino acid residues in chain Z^1 being counted from the C-terminal amino acid, whereby these amino acid residues are

- if n is 4 and n' is 6 the amino acid residues in positions 1 to 4 of the chain Z and in positions 1' to 6' in chain Z^1 are:

- P1: Tyr or Arg;
- P2: L-citrulline (Cit) or Arg;
- P3: Cys;
- P4: Arg-NH_2;

- P1': Lys or Arg;
- P2': Tyr;
- P3': Cys;
- P4': L-2-naphthylalanine (2-Nal);
- P5': Arg; and
- P6': Arg;

- Cys at P3 and P3' can form a disulfide bridge;

and

- if n is 5 and n' is 7, the amino acid residues in positions 1 to 5 in chain Z and in positions 1' to 7' in chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg or Arg-NH_2

- P1': Lys;
- P2': Cit;

- P3': Tyr;
- P4': Cys;
- P5': 2-Nal, Trp, L-para-aminophenylalanine (F(pNH_2)) or L-6-Cl-Tryptophan (W(6-Cl));
- P6': Arg;
- P7': ^{D}Arg, Arg, Ac-Arg, iPr-Arg, N-(2-aminoethyl)glycine ((EA)G), N-(3-aminopropyl)glycine ((PrA)G), N-(4-amino-n-butyl)glycine ((BA)G), N-(2-guanidinoethyl)glycine ((EGU)G), N-(3-guanidino-n-propyl)glycine ((PrGU)G), or N-(4-guanidino-n-butyl)glycine ((BGU)G);

Cys at P4 and P4' can form a disulfide bridge

or an enantiomer thereof or pharmaceutically acceptable salts thereof.

41-49. (Previously cancelled)

50. (Previously presented) The compound according to claim 40, wherein the α-amino acid residues in positions 1 to 4 of the chain Z and the α-amino acid residues in positions 1' to 6' chain Z^1 are:

- P1: Tyr, or Arg;
- P2: Cit, or Arg;
- P3: Cys;
- P4: Arg-NH_2;
- P1': Lys, orArg;
- P2': Tyr;
- P3': Cys;
- P4': 2-Nal;
- P5': Arg;
- P6': Arg; and

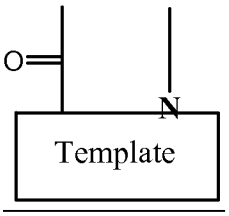
Cys at P3 and P3' can form a disulfide bridge.

51. (Previously presented) The compound according to claim 40, wherein the α-amino acid residues in positions 1 to 5 of the chain Z and the α-amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg, or Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal, Trp, F(pNH_2), or W(6-Cl);
- P6': Arg;
- P7`: ^{D}Arg, Arg, Ac-Arg, iPr-Arg, (EA)G, (PrA)G, (BA)G, (EGU)G, (PrGU)G, or (BGU)G; and

Cys at P4 and P4' can form a disulfide bridge.

52. (Currently amended) The compound of formula I according to claim 40, wherein

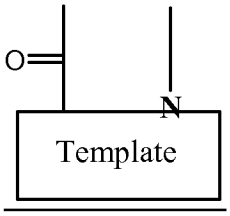


is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;

- P5: Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal;
- P6': Arg; and
- P7': Arg; and

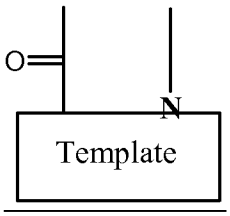
Cys at P4' and P4 forming a disulfide bridge.

53. (Currently amended) The compound of formula I according to claim 40, wherein ~~the~~ ~~template~~ 

is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal;
- P6': Arg; and-
- P7': Ac-Arg; and

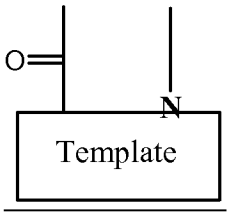
Cys at P4' and P4 forming a disulfide bridge.

54. (Currently amended) The compound of formula I according to claim 40, wherein ~~the~~ ~~template~~ 

is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal
- P6': Arg; and
- P7': ^{D}Arg; and

Cys at P4' and P4 forming a disulfide bridge.

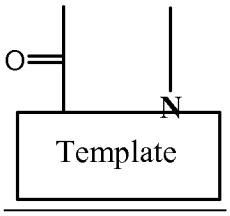
55. (Currently amended) The compound of formula I according to claim 40, wherein ~~the~~ ~~template~~ 

is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;

- P3: Cit;
- P4: Cys;
- P5: Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': Phe(pNH_2);
- P6': Arg; and
- P7': Arg; and

Cys at P4' and P4 forming a disulfide bridge.

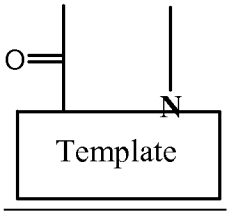
56. (Currently amended) The compound of formula I according to claim 40, wherein ~~the~~ ~~template~~ 

is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg-NH_2;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal;
- P6': Arg; and

- P7': (PrA)G; and

Cys at P4' and P4 forming a disulfide bridge.

57. (Currently amended) The compound of formula I according to claim 40, wherein ~~the~~ ~~template~~ 

is ^{D}Pro-^{L}Pro, n is 5, n' is 7 and the amino acid residues in positions 1 to 5 of the chain Z and the amino acid residues in positions 1' to 7' chain Z^1 are:

- P1: Tyr;
- P2: Arg;
- P3: Cit;
- P4: Cys;
- P5: Arg;
- P1': Lys;
- P2': Cit;
- P3': Tyr;
- P4': Cys;
- P5': 2-Nal;
- P6': Arg; and
- P7': Arg; and

Cys at P4' and P4 forming a disulfide bridge.

58.-60. (Cancelled)

61. (Previously presented) A pharmaceutical composition containing a compound according to claim 40 and a pharmaceutically inert carrier.

62. (Currently amended) The composition according to claim 61 in a form suitable for a mode of administration selected from the group consisting of oral, topical, transdermal, injection, buccal, transmucosal, pulmonary and inhalation.

63. (Currently amended) The composition according to claim 61 in a form selected from the group consisting of tablets, dragees, capsules, solutions, liquids, gels, plaster, creams, ointments, syrup, slurries, suspensions, spray, nebuliser or suppositories.

64. (Currently amended) The composition according to claim 62 in a form selected from the group consisting of tablets, dragees, capsules, solutions, liquids, gels, plaster, creams, ointments, syrup, slurries, suspensions, spray, nebuliser or suppositories.

65. (Previously presented) A method for treating a disorder mediated by or resulting from CXCR4 activity which comprises:

administering to a subject in need of such treatment an effective amount of a compound according to claim 40.

66. (Currently amended) A process for the manufacture of compounds according to claim 40, which process comprises

(a) coupling an appropriately functionalized solid support with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position 4 of Z if n is 4 or in position 5 of Z if n is 5, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

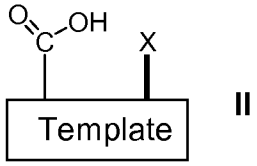
(b) removing the N-protecting group from the product thus obtained;

(c) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in Z of the desired end-product is one position nearer the N-terminal amino acid residue, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(d) removing the N-protecting group from the product thus obtained;

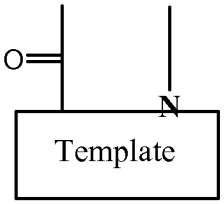
(e) repeating steps (c) and (d) until the N-terminal amino acid residue of Z has been introduced;

(f) coupling the product thus obtained with a compound of the general formula



II

wherein



is as defined in claim 40 and X is an N-protecting group; or, alternatively,

(fa) coupling the product obtained in step (e) with an appropriately N-protected derivative of ^{L}Pro or ^{D}Pro;

(fb) removing the N-protecting group from the product thus obtained; and

(fc) coupling the product thus obtained with an appropriately N-protected derivative of ^{D}Pro and, respectively, ^{L}Pro;

(g) removing the N-protecting group from the product obtained in step (f) or (fc);

(h) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position 1 of Z^1, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(i) removing the N-protecting group from the product thus obtained;

(j) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is one position farther away from position 1 of Z^1, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(k) removing the N-protecting group from the product thus obtained;

(l) repeating steps (j) and (k) until all amino acid residues of Z^1 have been introduced;

(m) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and appropriately substituting the reactive group(s) thus liberated;
(n) if desired, forming one or two interstrand linkage(s) between side-chains of appropriate amino acid residues at opposite positions of the β-strand region;
(o) detaching the product thus obtained from the solid support and removing any protecting groups present on functional groups of any members of the chain of amino acid residues and, if desired, any protecting group(s) which may in addition be present in the molecule; and
(p) if desired, converting the product thus obtained into a pharmaceutically acceptable salt or converting a pharmaceutically acceptable, or unacceptable, salt thus obtained into the corresponding free compound of formula I or into a different, pharmaceutically acceptable, salt.

67. (Cancelled)

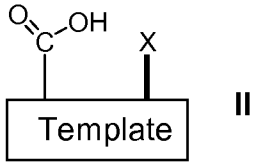
68. (Currently amended) ~~A~~ The process according to claim 67 wherein the leaving group in said leaving group-containing acylating agent is bromo, chloro or iodo acetic acid.

69-70. (Cancelled)

71. (New) A process for the manufacture of compounds according to claim 40, which process comprises:
(a) coupling an appropriately functionalized solid support with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position 4 of Z if n is 4 or in position 5 of Z if n is 5, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;
(b) removing the N-protecting group from the product thus obtained;
(c) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in Z of the desired end-product is one position nearer the N-terminal amino acid residue, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;
(d) removing the N-protecting group from the product thus obtained;

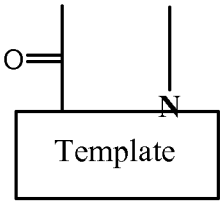
(e) repeating steps (c) and (d) until the N-terminal amino acid residue of Z has been introduced;

(f) coupling the product thus obtained with a compound of the general formula



II

wherein



is selected from the group consisting of ^{D}Pro-^{L}Pro and ^{L}Pro-^{D}Pro and X is an N-protecting group; or, alternatively,

(fa) coupling the product obtained in step (e) with an appropriately N-protected derivative of ^{L}Pro or ^{D}Pro;

(fb) removing the N-protecting group from the product thus obtained; and

(fc) coupling the product thus obtained with an appropriately N-protected derivative of ^{D}Pro and, respectively, ^{L}Pro;

(g) removing the N-protecting group from the product obtained in step (f) or (fc);

(h) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position 1 of Z^1, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(i) removing the N-protecting group from the product thus obtained;

(j) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is one position farther away from position 1 of Z^1, any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(k) removing the N-protecting group from the product thus obtained;

(l) repeating steps (j) and (k) until all amino acid residues of Z^1 have been introduced;

(m) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and appropriately substituting the reactive group(s) thus liberated;
(n) if desired, forming one or two interstrand linkage(s) between side-chains of appropriate amino acid residues at opposite positions of the β-strand region;
(o) detaching the product thus obtained from the solid support and removing any protecting groups present on functional groups of any members of the chain of amino acid residues and, if desired, any protecting group(s) which may in addition be present in the molecule; and
(p) if desired, converting the product thus obtained into a pharmaceutically acceptable salt or converting a pharmaceutically acceptable, or unacceptable, salt thus
obtained into the corresponding free compound of formula I or into a different, pharmaceutically acceptable, salt;

but wherein a residue of glycine having the amino group substituted by a chain having a polar-cationic residue is introduced by coupling with a leaving group-containing acylating agent, followed by nucleophilic displacement with an amine having the amino group substituted by a chain having a polar-cationic residue which, if necessary, is appropriately protected.

REPLACE the ABSTRACT with the following:

Template-fixed ß-hairpin peptidomimetics of the General Formula (I); wherein Z^1 and Z^2 are template-fixed chains of 4 and 6 or 5 and 7 α-amino acid residues and salts thereof. They have CXCR4-antagonizing properties and can be used as medicaments. These ß-sheet peptidomimetics can be manufactured by a process which is based on a mixed solid- and solution phase synthetic strategy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654